Editorial

Pandemics and the neurological manifestations of viral respiratory illnesses including Covid-19.

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Christie, Vicki and Dawn raise some really valid and pertinent thoughts and as I reflect on their guest editorial in our current Global crisis, the nexus between my two own areas of specialty becomes increasingly pellucid. After leaving clinical neuroscience practice for academia, immunisation and public health intervention is the mainstay of my clinical practice. Preventative health care measures have never been so imperative. From hand hygiene, cough etiquette and the elusive Covid-19 (SARS-CoV2) vaccine we are exposed to unparalleled and extraordinary media and social media coverage (Khan, Ali, Siddique, & Nabi, 2020). The current Covid-19 health crisis is stretching our health resources, nurses and medical staff to their absolute limits. Until recently it has been neurotropic viruses such as the measles virus that have generally been associated with central nervous system pathologies. However respiratory viruses including influenza and coronaviruses are emerging with neuropathological elements (Bohmwald, Gálvez, Ríos, & Kalergis, 2018). So what do we know about the history and impact of pandemics and how do novel respiratory viruses relate to neuroscience?

Viral respiratory illnesses and pandemics have been described since as early as 412BC. We are all familiar with the 1918 H1N1 (Spanish flu) influenza pandemic, but we often forget about the 1957 H2N2 (Asian flu) or the 1968 H3N2 (Hong Kong flu) influenza pandemics that both resulted in millions of lives lost. Our next influenza pandemic did not occur for another 51 years and caught many unaware. In early March 2009 cases of a novel H1N1 influenza strain (that is believed to have originated from pigs) emerged in California and Mexico (Broadbent & Subbarao, 2011). By May 2009 the first cases of the colloquially named “swine flu” were diagnosed in Australia (Australian Government Department of Health and Ageing, 2009; Eastwood, Durrheim, Jones, & Butler, 2010). Those like myself that were working during this time will remember being individually fitted for P3 masks and getting a sticker ones name badge that indicated size and fit, with shelves filled with different shapes and sizes of masks. This is such a contrast to this pandemic, where mask shortages and equipment deprivations are being reported internationally. The H1N1/09 pandemic is described by some as being relatively benign (Kotsimbos et al., 2010). This in part is due to the launch of the H1N1 vaccination program using the Panvax® vaccine that became available a mere 6 months after the virus was first identified (Bishop, Murnane, & Owen, 2009; Eastwood et al., 2010). However, vaccination is not an easy fix and various iterations of the (H1N1)pdm09-like virus strain have been included internationally in the seasonal flu vaccinations since 2010 to keep the spread in check. No pandemic is the same and each presents unique challenges for Governments, health care services and the community (Kotsimbos et al., 2010). We are only at the beginning of this current Covid-19 journey and still in a phase where we are working to contain and sustain our resources. Protection through a potential vaccine is still a long way off and likely to take years before control is effective.

Like influenza, coronaviruses are a group of related viruses that are zoonotic and primarily cause respiratory symptoms in humans (Chen et al., 2020; Su et al., 2016). Unlike influenza, there are no antiviral drugs or vaccines to treat or prevent human coronavirus infections. Coronaviruses are relatively new, having been first discovered in animals in the 1930’s, with the common cold the first human coronavirus discovered in the 1960’s (Kirkpatrick, 1996; Su et al., 2016). Covid-19

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is the third serious coronavirus outbreak to occur in the last 20 years, following the 2003 severe acute respiratory syndrome (SARS) and 2012 Middle East respiratory syndrome (MERS) outbreaks (LeDuc & Barry, 2004; Yang et al., 2020). Influenza and coronaviruses share many similarities, including the manifestation of neurological symptoms associated with poor outcomes (Li, Bai, & Hashikawa, 2020; Mao et al., 2020; Talan, 2020). It is not clear whether these symptoms and subsequent neurological events are a direct cause of the virus entering the central nervous system, or an indirect response to an overwhelming systemic viral storm (Fitzgerald, 2020). The most likely mode of infection is either a haematogenous or retrograde neuronal route (Mao et al., 2020).

Around 73% of Covid-19 cases are reported as being mild, however for the 18% of individuals who present with severe symptoms (Tian et al., 2020), the likelihood of neurological symptoms and complications increases. Mao et al. (2020) were among the first to report the prevalence of neurological symptoms associated with Covid-19, with 36% of individuals within their hospital-based cohort experiencing neurological symptoms. Clinical neurological manifestations include mild symptoms such as headache, dizziness and ataxia, myalgia (Lai, Shih, Ko, Tang, & Hsueh, 2020; Li et al., 2020; Mao et al., 2020; Talan, 2020), as well as more significant subsequent neurological events including altered level of consciousness, stroke, seizures, encephalopathy and central respiratory failure (Chen et al., 2020; Mao et al., 2020). Post-viral immune mediated complications such as acute disseminated encephalomyelitis and Guillain-Barré syndrome are also reported (Talan, 2020). Hypoxic encephalopathy associated with viral infections is often intractable and associated with an acute and rapid neurological deterioration (Achiriloaie et al., 2016). The spread of viruses via a synapse-connected route to the brainstem, including the medullary cardiorespiratory centre, is potentially partially responsible for acute respiratory failure (Khan et al., 2020; Li et al., 2020; Matsuda et al., 2004). Rates of hypoxic encephalopathy, as high as 20% in hospitalised cohorts (Chen et al., 2020), are also similar to previous influenza studies (Newland et al., 2007).

We are only just beginning to learn about Covid-19's various manifestations and complications. Whilst it is too early to make definite statements, the neuroinvasive propensity of Covid-19 has been well documented and not unexpected from our knowledge of influenza and other coronaviruses. Defined as "the greatest medical holocaust in history" (Waring, 1964), the 1918 pandemic of Spanish flu may yet be surpassed. Covid-19 has resulted in a worst-case scenario where lives are dominated by not only loss but also by unimaginable social and economic privation. So, now is the time to advance our awareness and to share our nursing knowledge with each other. We are already seeing that Covid-19 does not limit infection to the cardiorespiratory system. While the overall mortality of Covid-19 is lower than that of both SARS and MERS, its atypical symptoms, rapid person to person transmission and international spread is making it more deadly (Chen et al., 2020). It will be our awareness and close attention to neurological manifestations that will enable swift intervention and the possible saving of lives.

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References

Achiriloaie, A., Michelson, D., Lei, L., Denham, L., Oberg, K., & Raghavan, R. (2016). Acute Postviral Encephalopathy: Pathologic and Radiologic Correlation in an Atypical Case. *Child neurology open, 3*. doi:10.1177/2329048X16658845

Australian Government Department of Health and Ageing. (2009). Pandemic (H1N1) 2009 update bulletin. 13 October 2009. . Retrieved from http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/updates

Bishop, J. F., Murnane, M. P., & Owen, R. (2009). Australia's Winter with the 2009 Pandemic Influenza A (H1N1) Virus. *New England Journal of Medicine, 361*(27), 2591-2594. doi:10.1056/NEJMp0910445

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Bohmwald, K., Gálvez, N. M. S., Ríos, M., & Kalergis, A. M. (2018). Neurologic Alterations Due to Respiratory Virus Infections. *Frontiers in Cellular Neuroscience, 12*(386). doi:10.3389/fncel.2018.00386

Broadbent, A. J., & Subbarao, K. (2011). Influenza virus vaccines: lessons from the 2009 H1N1 pandemic. *Current opinion in virology, 1*(4), 254-262. doi:10.1016/j.coviro.2011.08.002

Chen, T., Wu, D., Chen, H., Yan, W., Yang, D., Chen, G., . . . Ning, Q. (2020). Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ, 368*, m1091. doi:10.1136/bmj.m1091

Eastwood, K., Durrheim, D. N., Jones, A., & Butler, M. (2010). Acceptance of pandemic (H1N1) 2009 influenza vaccination by the Australian public. *Medical Journal of Australia, 192*(1), 33-36. doi:10.5694/j.1326-5377.2010.tb03399.x

Fitzgerald, S. (2020). The Spread of COVID-19: Questions Raised, Some Answered by Neuroinfectious Disease Experts. *Neurology Today, March*.

Khan, S., Ali, A., Siddique, R., & Nabi, G. (2020). Novel coronavirus is putting the whole world on alert. *Journal of Hospital Infection, 104*(3), 252-253. doi:10.1016/j.jhin.2020.01.019

Kirkpatrick, G. L. (1996). The common cold. *Primary Care: Clinics in Office Practice, 23*(4), 657-675. doi:10.1016/S0095-4543(05)70355-9

Kotsimbos, T., Waterer, G., Jenkins, C., Kelly, P. M., Cheng, A., Hancox, R. J., . . . Thompson, P. (2010). Influenza A/H1N1_09: Australia and New Zealand's Winter of Discontent. *American Journal of Respiratory and Critical Care Medicine, 181*(4), 300-306. doi:10.1164/rccm.200912-1878CP

Lai, C.-C., Shih, T.-P., Ko, W.-C., Tang, H.-J., & Hsueh, P.-R. (2020). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *International Journal of Antimicrobial Agents, 55*(3), 105924. doi:10.1016/j.ijantimicag.2020.105924

LeDuc, J. W., & Barry, M. A. (2004). SARS, the First Pandemic of the 21st Century. *Emerging Infectious Diseases, 10*(11), e26-e26. doi:10.3201/eid1011.040797_02

Li, Y. C., Bai, W. Z., & Hashikawa, T. (2020). The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*. doi:10.1002/jmv.25728

Mao, L., Wang, M., Chen, S., He, Q., Chang, J., Hong, C., . . . Hu, B. (2020). Neurological Manifestations of Hospitalized Patients with COVID-19 in Wuhan, China: a retrospective case series study. *medRxiv*, Epub. doi:10.1101/2020.02.22.20026500

Matsuda, K., Park, C. H., Sunden, Y., Kimura, T., Ochiai, K., Kida, H., & Umemura, T. (2004). The vagus nerve is one route of transneural invasion for intranasally inoculated influenza a virus in mice. *Vet Pathol, 41*(2), 101-107. doi:10.1354/vp.41-2-101

Newland, J. G., Laurich, V. M., Rosenquist, A. W., Heydon, K., Licht, D. J., Keren, R., . . . Coffin, S. E. (2007). Neurologic complications in children hospitalized with influenza: characteristics, incidence, and risk factors. *J Pediatr, 150*(3), 306-310. doi:10.1016/j.jpeds.2006.11.054

Su, S., Wong, G., Shi, W., Liu, J., Lai, A. C. K., Zhou, J., . . . Gao, G. F. (2016). Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. *Trends Microbiol, 24*(6), 490-502. doi:10.1016/j.tim.2016.03.003

Talan, J. (2020). COVID-19: Neurologists in Italy to Colleagues in US: Look for Poorly-Defined Neurologic Conditions in Patients with the Coronavirus. *Neurology Today, March*.

Tian, S., Hu, N., Lou, J., Chen, K., Kang, X., Xiang, Z., . . . Zhang, J. (2020). Characteristics of COVID-19 infection in Beijing. *Journal of Infection, 80*(4), 401-406. doi:10.1016/j.jinf.2020.02.018

Waring, J. I. (1964). *A History of Medicine in South Carolina: 1900-1970* (Vol. 3): South Carolina Medical Association.

Yang, Y., Peng, F., Wang, R., Guan, K., Jiang, T., Xu, G., . . . Chang, C. (2020). The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China. *Journal of Autoimmunity*, 102434. doi:10.1016/j.jaut.2020.102434

Help determine the impact of COVID-19 on neurocritical care by participating in research.

The Neuro Critical Care Society has developed an international collaborative using common data elements for a number of studies. If you are interested in collaborating with these efforts. Please see https://www.neurocriticalcare.org/research/covid-19-research-opportunities